The Dow Chemical Company
Midland, MI 48674
USA

2020 DOW CENTER

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CONFIDENTIAL BUSINESS INFORMATION 40 CFR 2.201-2.215

VIA CDX

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(Attn: TSCA Section 8(e) Coordinator)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20004-3302

Generic Name: Bis-Heterocyclic Amide

The following information is being submitted by The Dow Chemical Company (Dow) pursuant to current guidance issued by EPA indicating EPAâs interpretation of Section 8(e) of the Toxic Substances Control Act. Dow has made no determination as to whether a significant risk of injury to health or the environment is actually presented by the findings.

During a dietary toxicology study male and female beagle dogs, 2/sex/day were exposed to 2000 or 4000 ppm in feed for 28 days,

All male and female dogs given 4000 ppm lost body weight relative to their pre-study body weight over the course of the study. At the end of the 28-day exposure period, the two male dogs given 4000 ppm had lost 9 and 12% of their body weight, and the two female dogs given 4000 ppm had lost 8 and 9% of their body weight. Individual animal food consumption values were generally lower in both sexes at 4000 ppm in comparison with the 2000 ppm group during the targeted dosing period. This decrease in food consumption at 4000 ppm was considered to be related to the test material in the feed, resulting in lower body weights.

A histopathologic observation that was potentially related to administration of the test material was noted in the bone marrow of one male given 4000 ppm. This effect consisted of

moderate myeloid cell hyperplasia. The hyperplasia was characterized by increased myeloid precursors, primarily myeloblasts through the band neutrophil stage. The number of mature neutrophils in the marrow was disproportionately low as compared to the number of neutrophil precursors, indicative of ineffective myelopoiesis with a relative maturation arrest at the band neutrophil stage. A corresponding hematologic alteration consisted of a marked decrease in circulating neutrophils on day 28, relative to the pretest value. This dog also had microscopic liver observations which consisted of very slight extramedullary hematopoiesis, very slight diffuse hyperplasia and hypertrophy of Kupffer cells, and slight diffuse hepatocellular vacuolization consistent with fatty change.

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The liver of one female given 4000 ppm had very slight hepatocellular vacuolization consistent with fatty change. The fatty change of the liver in these two high-dose animals was interpreted to be related to the loss of body weight that occurred during the study.

At the day 14 and day 28 blood collections, there were mild increases in alkaline phosphatase (ALP) in all treated animals (up to +255%), relative to individual pretest values. Mild decreases in alanine aminotransferase (ALT) were also present in all treated animals (up to -63%), and mild decreases in aspartate aminotransferase (AST) were present in both sexes administered 4000 ppm (up to -33%), relative to individual pretest values. The alterations in ALP, ALT and AST tended to slightly progress from the day 14 to the dy 28 collections, and were likely treatment-related.

Questions may be addressed to the undersigned.

Sincerely,

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